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8EHQ-1204-15886

Great Lakes
CHEMICAL CORPORATION

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Attention: TSCA Section 8(e) Coordinator

RE: Submission of Reproductive and Fetal Survival Effects in the Rat via an OECD 421 Guideline Screening Study of Phenol, isopropylated, phosphate (3:1); (CAS No.: 68937-41-7) [
].
(When responding, please refer to JAB-04-069).

Dear Sir:

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Great Lakes Chemical Corporation (GLCC) submits this letter of substantial risk notification in accordance with Section 8(e) of the Toxic Substances Control Act, 15 USC 2607(e), and the Environmental Protection Agency's "Statement of Interpretation and Enforcement Policy" thereof 43 FR 1110, 35 seq., March 16,1978. The notification is in regards to a verbal report and draft Summary Data Tables received from the laboratory that is performing an OECD 421 the Reproduction/ Developmental Toxicity Screening Test of isopropylated triphenyl phosphate (common name) [
].

The test material was administered via oral gavage using corn oil as the carrier vehicle to a group of 12 male and 12 female rats of the Sprague-Dawley Crl:CD*(SD)IGS BR strain. The test material was given once daily at the dose level of 400 mg/kg. Males were dosed for at least 14 days prior to mating which continued throughout the 14 day mating period and for at least 14 days after completion of the mating period until all conceived females delivered. Females were dosed for at least 14 days prior to mating, throughout mating and continued to be dosed until one day prior to termination (lactation day 4 for those that delivered, post-mating day 25 or post-cohabitation day 25 for those that did not deliver). A concurrent control group of identical design received the carrier vehicle corn oil on a comparable regimen.

The study design included recording F_0 viability and clinical observations, food consumption, body weights, and parturition and litter observations. Macroscopic examinations were conducted on all F_0 animals with tissues and organs collected for microscopic examination and relative organ weight determination in accordance with the study protocol. F_1 data included litter identification, pup body weights, and appearance and behavior observations. All F_1 pups

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were examined macroscopically and preserved intact in Bouin's solution for possible future whole-body visceral evaluation.

Fertility of the test group is considered comparable with that of the control group. All 12 animals were pregnant, as were the animals of the control group. However, one test animal expired during delivery and, therefore, did provide a litter. The test group means for number of live and total pups delivered were comparable with the control group. However, the mean number of pups delivered dead was increased and the mean number of surviving pups at lactation day 4 (study termination) was decreased, when compared to the control group.

There were statistically significant effects noted for body weight and absolute and/or relative organ weights in test males, when compared to the control. The mean body weight was decreased ($p<0.05$). The mean absolute (A) and/or relative (R) organ weights that were affected include liver (increased A & R), epididymides (decreased A) and adrenal glands (increased A & R). Significant difference was $p<0.01$ for adrenal glands (A & R) and liver (R) and was $p<0.05$ for epididymides (A) and liver (R). In the females both the mean absolute and relative organ weights of liver were statistically significantly increased ($p<0.01$).

Sincerely,

John A. Biesemeier
Manager, Regulatory Toxicology
Regulatory Affairs

JAB/jab